AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph [018] with the following rewritten paragraph:

— **[018]** FIG. 1 (SEQ ID NOS:1-26) depicts CD8 α-chain protein and nucleic acid sequences from various species. Also included are accession numbers for the noted sequences. —

Please replace the paragraph [019] with the following rewritten paragraph:

— **[019]** FIGS. 2A-B (SEQ ID NOS:27-30) depict the amino acid and nucleic acid sequences for the wild-type CD8 α-chain, including a demarcation of the different domains of the protein for the human and mouse. —

Please replace the paragraph [032] with the following rewritten paragraph:

— **[032]** FIG 15 (SEQ ID NO:31) Depicts the mRNA sequence of Hemoglobin β. —

Please replace the paragraph [033] with the following rewritten paragraph:

— **[033]** FIG 16 (SEQ ID NO:32) Depicts the mRNA sequence of GATA binding protein. —

Please replace the paragraph [034] with the following rewritten paragraph:

— **[034]** FIG 17 (SEQ ID NO:33) Depicts the mRNA sequence of d-aminoevulinate synthase. —

Please replace the paragraph [035] with the following rewritten paragraph:

— **[035]** FIG 18 (SEQ ID NO:34) Depicts the mRNA sequence of Glucose-6-phosphate-dehydrogenase. —

Please replace the paragraph [036] with the following rewritten paragraph:

— **[036]** FIG 19 (SEQ ID NO:35) Depicts the mRNA sequence of Ornithine carbamoyl transferase. —

Please replace the paragraph [037] with the following rewritten paragraph:

— **[037]** FIG 20 (SEQ ID NO:36) depicts the mRNA sequence of α-L-iduronidase. —

Please replace the paragraph [038] with the following rewritten paragraph:

— **[038]** FIG 21 (SEQ ID NO:37) depicts the mRNA sequence of β-glucosidase. —

Please replace the paragraph [039] with the following rewritten paragraph:

— **[039]** FIG 22 (SEQ ID NO:38) depicts the mRNA sequence of α-galactosidase. —

Please replace the paragraph [056] with the following rewritten paragraph:

— **[056]** Preferred diseases that may be treated by the methods and compositions disclosed herein are set forth in Table 1 below. The sequences provided with the accession numbers are expressly incorporated herein by reference.

TABLE 1

Gene Therapy Targets			
Disease Name	**Defect**	**Accession Number/mRNA**	**SEQ ID NO:**
Sickle Cell Anemia	hemoglobin-β	NM_000518	SEQ ID NO:31
x-linked Dyserythropoietic Anemia	GATA-binding protein	NM_002049	SEQ ID NO:32
Sideroblastic Anemia	δ-aminoevulinate synthase	NM_000032	SEQ ID NO:33
Chronic Hemolytic Anemia (Favism)	glucose-6-phosphate-dehydrogenase	NM_000402	SEQ ID NO:34
Hemophilia A	Coagulation Factor VIII	NM_000132	SEQ ID NO:39
Hemophilia B	Coagulation Factor XI	NM_000133	SEQ ID NO:40
Cystic Fibrosis	cystic fibrosis transmembrane conductance regulator	NM_000492	SEQ ID NO:41
OTC-Deficiency	ornithine carbamoyl transferas	NM_000531	SEQ ID NO:35
Hurler Syndrome	α-L-iduronidase	NM_000203	SEQ ID NO:36
Hunter Syndrome	iduronate-2-sulfatase	NM_000202	SEQ ID NO:42
Gaucher Disease	β-glucosidase	NM_000157	SEQ ID NO:37

Fabry Disease	α-galactosidase	NM_000169	SEQ ID NO:38
Krabbe Disease	galactosylceramidase	NM_000153	SEQ ID NO:43
Pompe Disease	acid α-glucosidase	NM_000152	SEQ ID NO:44
Tay-Sachs Disease	hexamidase A	NM_000520	SEQ ID NO:45
Phenylketonuria	phenylalanine hydroxylase	NM_000277	SEQ ID NO:46
Alport Syndrome	collagen type IV, α5	NM_000495	SEQ ID NO:47
Bloom Syndrome	Bloom Sundrome Gene Product	NM_000057	SEQ ID NO:48
Familial Hypercholestrolemia	low density lipoprotein receptor	NM_000527	SEQ ID NO:49

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Please replace the paragraph [066] with the following rewritten paragraph:

— **[066]** As will be appreciated by those of skill in the art the transmembrane domain of the CD8 α-chain can be exchanged with transmembrane domains of other molecules, if necessary, to modify association of the extracellular domain with the target cell surface. In this embodiment the nucleic acid encoding the extracellular domain of CD8 α-chain is operably linked to a nucleic acid encoding a transmembrane domain. Transmembrane domains of any transmembrane protein can be used in the invention. Alternatively a transmembrane not known to be found in transmembrane proteins. In this embodiment the "synthetic transmembrane domain" contains from around 20 to 25 hydrophobic amino acids followed by at least one and preferably two charged amino acids. In some embodiments the CD8 extracellular domain is linked to the target cell membrane by conventional techniques in the art. Preferred CD8 α-chain sequences are set forth in Figure 1 (SEQ ID NOS:1-26) and include the full length sequences of either the amino acid sequence or nucleic acid sequence encoding a full length CD8 α-chain from species including human, mouse, rat, orangutan, spider monkey, guinea pig, cow, Hispid cotton rat, domestic pig and cat. —

Please replace the paragraph [067] with the following rewritten paragraph:

— **[067]** In a preferred embodiment the CD8 α-chain is not a fusion protein, but rather is a truncation protein wherein the intracellular domain is deleted. As depicted in Figure 2 (SEQ ID

NOS:27-30), the human CD8 α-chain gene expresses a protein of 235 amino acids. The protein can be considered to be divided into the following domains (starting at the amino terminal and ending at the carboxy terminal of the polypeptide): a signal peptide (amino acids 1 to 21); immunoglobulin (Ig)-like domain (approximately amino acids 22-136); membrane proximal stalk region (amino acids 137-181); transmembrane domain (amino acids 183-210) and cytoplasmic domain (amino acids 211-235). The nucleotides of the coding sequence that encode these different domains include 1-63 encoding the signal peptide, 64-546 encoding the extracellular domain, about 547-621 encoding the intracellular domain and about 622-708 encoding the intracellular domain. Likewise, the mouse sequences can be divided into domains as follows. The polypeptide can be divided into a signal sequence including amino acids 1-27, an extracellular domain including about amino acids 28 to 194, a transmembrane domain including about amino acids 195-222 and an intracellular domain including about amino acids 223-310. Similarly, the nucleotides of the coding sequence encoding these domain include nucleic acid 1-81 encoding the signal peptide, about 82-582 encoding the extracellular domain, about 583-666 encoding the transmembrane domain and about 667-923 encoding the extracellular domain. —

Please replace the paragraph [069] with the following rewritten paragraph:

— **[069]** One skilled in the art will also appreciate that immunomodulatory molecules having substantial homology to the afore-mentioned polypeptides may find advantageous use in the invention. Accordingly, for example, also encompassed by "CD8 polypeptides" are homologous polypeptides having at least about 80% sequence identity, usually at least about 85% sequence identity, preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity and most preferably at least about 98% sequence identity with the polypeptide encoded by nucleotides shown in Figure 2 (SEQ ID NOS:27 and SEQ ID NO:29). —

Please replace the paragraph [070] with the following rewritten paragraph:

— **[070]** By "nucleic acid molecules encoding CD8", and grammatical equivalents thereof is meant the nucleotide sequence of human CD8 as shown in Figure 2 (SEQ ID NOS:28) as well as nucleotide sequences having at least about 80% sequence identity, usually at least about 85%

sequence identity, preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity and most preferably at least about 98% sequence identity with nucleotides shown in Figure 2 (SEQ ID NO:28 and SEQ ID NO:30) and which encode a polypeptide having the sequence shown in Figure 2 (SEQ ID NO:27 and SEQ ID NO:29), and as set forth in Figure 1 (SEQ ID NOS:1-26). —

Please replace the paragraph [078] with the following rewritten paragraph:

— **[078]** CD8 having less than 100% sequence identity with the polypeptide encoded by nucleotides in Figure 2 (SEQ ID NO:27 and SEQ ID NO:29) will generally be produced from native CD8 nucleotide sequences from species other than human and variants of native CD8 nucleotide sequences from human or non-human sources. In this regard, it is noted that many techniques are well known in the art and may be routinely employed to produce nucleotide sequence variants of native CD8 sequences and assaying the polypeptide products of those variants for the presence of at least one activity that is normally associated with a native CD8 polypeptide. In a preferred embodiment the CD8 α-chain is from human but as shown in Figure 1 (SEQ ID NOS:1-26), CD8 α-chain from rat, mouse, and primates are known and find use in the invention. —

Please replace the paragraph [079] with the following rewritten paragraph:

— **[079]** Polypeptides having CD8 activity may be shorter or longer than the polypeptide encoded by nucleotides depicted in Figure 2 (SEQ ID NO:27 and SEQ ID NO:29). Thus, in a preferred embodiment, included within the definition of CD8 polypeptide are portions or fragments of the polypeptide encoded by nucleotides in Figure 2. In one embodiment herein, fragments of the polypeptide encoded by nucleotides in Figure 2 are considered CD8 polypeptides if a) they have at least the indicated sequence identity; and b) preferably have a biological activity of naturally occurring CD8, as described above. —

Please replace the paragraph [080] with the following rewritten paragraph:

— **[080]** In addition, as is more fully outlined below, CD8 α-chain can be made longer than the polypeptide encoded by nucleotides in Figure 2 (SEQ ID NO:27 and SEQ ID NO:29); for example, by the addition of other fusion sequences, or the elucidation of additional coding and non-coding sequences. —

Please replace the paragraph [081] with the following rewritten paragraph:

— **[081]** The CD8 polypeptides are preferably recombinant. A "recombinant polypeptide" is a polypeptide made using recombinant techniques, i.e. through the expression of a recombinant nucleic acid as described below. In a preferred embodiment, CD8 of the invention is made through the expression of nucleic acid sequence shown in Figure 2 (SEQ ID NO:28 and SEQ ID NO:30), or fragment thereof. A recombinant polypeptide is distinguished from naturally occurring protein by at least one or more characteristics. For example, the polypeptide may be isolated or purified away from some or all of the proteins and compounds with which it is normally associated in its wild type host, and thus may be substantially pure. For example, an isolated polypeptide is unaccompanied by at least some of the material with which it is normally associated in its natural state, preferably constituting at least about 0.5%, more preferably at least about 5% by weight of the total protein in a given sample. A substantially pure polypeptide comprises at least about 75% by weight of the total polypeptide, with at least about 80% being preferred, and at least about 90% being particularly preferred. The definition includes the production of a CD8 polypeptide from one organism in a different organism or host cell. —

Please replace the paragraph [083] with the following rewritten paragraph:

— **[083]** In one embodiment, the present invention provides nucleic acid CD8 variants. These variants fall into one or more of three classes: substitutional, insertional or deletional variants. These variants ordinarily are prepared by site specific mutagenesis of nucleotides in nucleotides of Figure 2 (SEQ ID NO:28 and SEQ ID NO:30), using cassette or PCR mutagenesis or other techniques well known in the art, to produce DNA encoding the variant, including the variant in a gene therapy vector and thereafter expressing the DNA. Amino acid sequence variants are

characterized by the predetermined nature of the variation, a feature that sets them apart from naturally occurring allelic or interspecies variation of CD8 amino acid sequence. The variants typically exhibit the same qualitative biological activity as the naturally occurring analogue, although variants can also be selected which have modified characteristics as will be more fully outlined below. —

Please replace the paragraph [156] with the following rewritten paragraph:

— **[156]** Use of the subject compositions and methods to specifically inhibit alloimmune and autoimmune responses is described in co-pending U.S. Patent Application Serial No. ~~XX~~ 10/804,762, the disclosure of which is incorporated by reference herein in its entirety. Other applications of the method and compositions of the present invention will be apparent to those skilled in the art. —

Please replace the paragraph [0187] with the following rewritten paragraph:

— **[0187]** As control vector expressing the bacterial LacZ gene (β-galactosidase) the Qbiogene provided QBI-Infect+ Viral Particle (Ad5.CMVLacZΔE1/ΔE3). Mouse CD8 α-chain sequence used. This sequence is similar to the published mouse sequence:

ACTUAL SEQUENCE: MASPLTRFLS LNLLLMGESI

ILGSGEAKPQAPELRIFPKK MDAELGQKVD LVCEVLGSVS QGCSWLFQNS

SSKLPQPTFVVYMASSHNKI TWDEKLNSSK LFSAVRDTNN KYVLTLNKFS

KENEGYYFCSVISNSVMYFS SVVPVLQKVN STTTKPVLRT PSPVHPTGTS

QPQRPEDCRPRGSVKGTGLD FACDIYIWAP LAGICVAPLL SLIITLICYH

RSRKRVCKCPRPLVRQEGKP RPSEKIV (SEQ ID NO:50). —

Please replace the paragraph [0188] with the following rewritten paragraph:

— **[0188]** Human CD8 α-chain sequence used. This sequence has a silent mutation compared to the published human sequence as indicated.

ACTUAL SEQUENCE: MALPVTALLL PLALLLHAAR PSQFRVSPLDRTWNLGWTVE LKCQVLLSNP TSGCSWLFQP RGAAASPTFL LYLSQNKPKAAEGLDTQRFS GKRLGDTFVL TLSDFRRENE GYYFCSALSN SIMYFSHFVPVFLPAKPTTT PAPRPPTPAP TIASQPLSLR PEACRPAAGG AGNRRRVCKCPRPVVKSGDK PSLARYV (SEQ ID NO:51). —

Please insert the enclosed 67-page text entitled "SEQUENCE LISTING" immediately preceding the claims.